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BERTAGNA, ANGELA MARIE				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/532,975

**Applicant(s)**

MITANI ET AL.

**Examiner**

ANGELA BERTAGNA

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17, 22 and 23 is/are rejected.
- 7) ☒ Claim(s) 1-3, 6, 9-12, 15, 22 and 23 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 7/21/08; 8/1/08; 9/11/08
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(c) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 21, 2008 has been entered.

***Status***

2. Claims 1-17, 22, and 23 are currently pending. In the response, Applicant amended claims 1-3, 6, 9-12, and 15, canceled claims 18-21, and added claims 22-23.

***Information Disclosure Statement***

3. Applicant's submission of an Information Disclosure Statement on July 21, 2008, August 1, 2008, and September 11, 2008 is acknowledged. Signed copies are enclosed.

It is noted that foreign patent citation #2 (JP 3-313358) on the IDS filed on July 21, 2008 has been lined through since the citation was not in compliance with 37 CFR 1.98(b)(4). This reference was properly cited on the IDS filed on August 1, 2008, and therefore, it was considered on this IDS. It is also noted that the IDS filed on August 1, 2008 contains duplicate citations of the references listed on the IDS filed on July 21, 2008. These references were considered on the IDS filed on July 21, 2008, and the duplicate citations appearing on the IDS filed on August 1, 2008 were lined through. It is also noted that minor corrections were made to several citations

appearing in the IDS filed on September 11, 2008. All of the references on this IDS were considered.

### *Claim Objections*

4. Claims 22 and 23 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 22 is drawn to the method of claim 1, wherein in the presence or the absence of an intervening sequence between sequences (Ac') and (B'), the value of  $(X+Y+Y')$  or  $(X+Y)$  is 100 or less. Claim 23 is drawn to the method of claim 9, wherein in the presence or the absence of an intervening sequence between sequences (Ac') and (B'),  $(X+Y+Y')$  or  $(X+Y)$  is 100 or less, and wherein in the presence or the absence of an intervening sequence between sequences (Cc') and (D'),  $(X+Y+Y')$  or  $(X+Y)$  is 100 or less. Since claims 1 and 9 recite that the values of  $(X+Y)$  and  $(X+Y+Y')$  are 30 or more in the presence or absence of an intervening sequence, the methods recited in new claims 22 and 23 fail to further limit the methods of claims 1 and 9.

Claims 1-3, 6, 9-12, and 15 are objected to because of the following informalities: These claims contain grammatical and/or typographical errors. The following changes are suggested:

(i) replacing "which" appearing in lines 18 and 20 of claim 1 and in lines 33, 36, 46, and 49 of claim 9 with "that",

(ii) inserting the word "to" in lines 18 and 20 of claim 1 and in lines 33, 36, 47, and 49 of claim 9 after the word "hybridizes",

- (iii) inserting a comma after "(Ac')" in line 20 of claim 1,
- (iv) deleting the word "the" appearing before "step" in steps (b) and (c) of claim 1,
- (v) deleting the word "the" appearing before "step" in claims 2, 3, 6, 9-12, and 15,
- (vi) deleting the words "a step of" in step (c) of claim 9, and
- (vii) replacing the phrase "another primers" in step (c) of claim 9 with "another primer" or "additional primers".

Appropriate correction is required.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph (New Matter)***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As noted in MPEP 2163.06 I, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Claim 23 is drawn to the method of claim 9, wherein in the presence or the absence of an intervening sequence between sequences (Ac') and (B'), (X+Y+Y') or (X+Y) is 100 or less, and

wherein in the presence or the absence of an intervening sequence between sequences (C'') and (D'), (X+Y+Y') or (X+Y) is 100 or less. Applicant indicates that this claim is supported by page 15, lines 6-7 of the specification (see page 8 of the response). This section of the specification describes primer lengths and lengths of sequences (A'') and (B'') within the primer that are suitable for practice of the invention. This section of the specification does not discuss the length of the region Y that is flanked by regions A and B in the target sequence, and therefore, it does not provide adequate support for the limitation "wherein (X+Y) is less than 100". It is noted that page 14 of the specification provides adequate support for values of (X+Y+Y') that are 100 or less (see lines 27-36). However, neither page 14 nor the remainder of the original disclosure provides adequate support for values of (X+Y) that are less than 100, and therefore, claim 23 has been rejected under 35 U.S.C. 112, first paragraph for incorporating new matter.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite, because it recites the limitation "the template nucleic acid" in line

2. There is insufficient antecedent basis for this limitation in the claim. There is sufficient antecedent basis for "the double-stranded template nucleic acid".

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-7, 9-16, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabbani et al. (EP 0 971 039 A2; cited previously) in view of Notomi et al. (Nucleic Acids Research 2000; 28(12): e63; cited previously).

These claims are drawn to an isothermal nucleic acid amplification method.

Regarding claim 1, Rabbani teaches a method for amplifying a nucleic acid comprising:

(a) annealing a primer to a template nucleic acid and synthesizing a complementary nucleic acid via primer extension,

wherein the primer comprises in its 3' end portion a sequence (Ac') that hybridizes to a sequence (A) in the 3' end portion of the target nucleic acid, and a sequence (B') located 5' of

(Ac') that hybridizes to the complementary sequence (Bc) of a sequence (B) positioned 5' of sequence (A) in the target nucleic acid (see Example 1 on page 21, especially paragraphs 120-121, where the FC and RC primers of Rabbani are taught; see also Figure 1, steps 1-2)

wherein in the absence of an intervening sequence between (Ac') and (B'),  $(X-Y)/X$  is between -1.00 and 1.00, where X is the number of bases in sequence (Ac') and Y is the number of bases in the region flanked by sequences (A) and (B) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Ac') region of 19 or 20 nucleotides and the region flanked by sequences A and B is 0 nucleotides, since there is no intervening sequence between them. Therefore,  $(X-Y)/X = 1$  and  $X+Y = 19$  or  $20$ )

(b) hybridizing sequence (B') with sequence (Bc) on the newly synthesized strand, thereby allowing sequence (A) on the target strand to be single-stranded (see Figure 1, step 3)

(c) annealing another primer of step (a) to the single-stranded sequence (A) on the target generated in step (d) and conducting a strand displacement reaction, thereby displacing the complementary nucleic acid synthesized in step (c) (see Figure 1, steps 4-5).

Regarding claim 2, Rabbani teaches that the double-stranded nucleic acid obtained in step (e) is used repeatedly in step (d) (see Figure 1 and paragraph 47).

Regarding claims 3 and 12, Rabbani teaches that the method is conducted isothermally (see paragraphs 46, 51, and 121).

Regarding claims 4 and 13, Rabbani teaches use of the Bst DNA polymerase, which has strand-displacing ability (paragraph 120).

Regarding claims 5 and 14, Rabbani teaches that the method further comprises a step of synthesizing cDNA with a reverse transcriptase from an RNA template (paragraph 111).



Regarding claims 6, 7, 15, and 16, Rabbani teaches conducting the method in the presence of a melting temperature adjusting agent, specifically formamide or DMSO (paragraph 39).

Regarding claim 9, Rabbani teaches a method for amplifying a target nucleic acid in a double-stranded template nucleic acid comprising:

(a) annealing first and second primers to first and second template nucleic acids of a double-stranded template nucleic acid and synthesizing first and second complementary strands via primer extension (see paragraphs 117-118; see also Figure 1, steps 1-2 for a schematic of how the primers anneal to the target. Although Figure 1 shows the reactions occurring on only one strand, when both the FC and RC primer are used with a double-stranded template as taught by Rabbani in Example 1, each of the primers inherently undergoes the reactions outlined in Figure 1 on a different strand of the template; see also paragraph 77, where Rabbani expressly teaches conducting the amplification method using two stem-loop primers each of which is complementary to a different strand of a double-stranded DNA template),

wherein the first primer comprises in its 3' end portion a sequence (Ac') that hybridizes to a sequence (A) in the 3' end portion of the target nucleic acid, and a sequence (B') located 5' of (Ac') that hybridizes to the complementary sequence (Bc) of a sequence (B) positioned 5' of sequence (A) in the target nucleic acid (see Example 1 on page 21, where the FC and RC primers of Rabbani are taught; see also Figure 1 for a schematic of the primers binding to a target; paragraphs 77 & 177 teach the use of double-stranded nucleic acid targets), and

wherein in the absence of an intervening sequence between (Ac') and (B'),  $(X-Y)/X$  is between -1.00 and 1.00, where X is the number of bases in sequence (Ac') and Y is the number

of bases in the region flanked by sequences (A) and (B) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Ac') region of 19 or 20 nucleotides and the region flanked by sequences A and B is 0 nucleotides, since there is no intervening sequence between them. Therefore,  $(X-Y)/X = 1$  and  $X+Y = 19$  or  $20$ ), and

wherein the second primer comprises in its 3' end portion a sequence (Cc') that hybridizes to a sequence (C) in the 3' end portion of the target nucleic acid, and a sequence (D') located 5' of (Cc') that hybridizes to the complementary sequence (Dc) of a sequence (D) positioned 5' of sequence (C) in the target nucleic acid (see Example 1 on page 21, where the FC and RC primers of Rabbani are taught; see also Figure 1 for a schematic of the primers binding to a target)

wherein in the absence of an intervening sequence between (Cc') and (D'),  $(X-Y)/X$  is between  $-1.00$  and  $1.00$ , where X is the number of bases in sequence (Cc') and Y is the number of bases in the region flanked by sequences (C) and (D) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Cc') region of 19 or 20 nucleotides and the region flanked by sequences C and D is 0 nucleotides, since there is no intervening sequence between them. Therefore,  $(X-Y)/X = 1$  and  $X+Y = 19$  or  $20$ )

(b) hybridizing the sequences (B') and (D') with the newly synthesized sequences (Bc) and (Dc), respectively, thereby making sequences (A) and (C) single stranded (see Figure 1, step 3 and paragraph 118; see also paragraph 77)

(c) annealing primers having the same sequence as the first and second primers of step (a) to sequences (A) and (C) obtained in step (e) above and conducting strand displacement

polymerization to displace the complementary strands obtained in step (d) and synthesize new complementary strands (see paragraph 118 and Figure 1, steps 4-5; see also paragraph 77).

Regarding claim 10, Rabbani teaches that the double-stranded nucleic acids obtained in step (f) are repeatedly used in step (c) (see paragraphs 77 & 118; see also Figure 1).

Regarding claim 11, Rabbani teaches that the first and second complementary nucleic acids obtained in step (f) as single-stranded nucleic acids are used repeatedly as template nucleic acids in step (d) (see Figure 2, step 4 and paragraph 77).

Regarding claims 22 and 23, the primers have an X+Y value of 19 or 20 in the absence of an intervening sequence between (Ac') and (B') or (Cc') and (D') (see above), which is less than 100.

In the method of Rabbani, the primers have an X+Y value of 19 or 20 (see above), which is outside of the range recited in independent claims 1 and 9 of 30 or more.

Notomi teaches a method for isothermally amplifying DNA using primers that form stem-loop structures after extension (see abstract, pages ii-iv, and Figure 1). Like the primers of Rabbani, the primers of Notomi comprise a region that is complementary to the template and a region that is complementary to a portion of the primer extension product (see pages ii-iv and Figure 1). Regarding claims 1 and 9, Notomi teaches that the size of the loop formed between the primer and the primer extension product (*i.e.* the claimed Y value) is critical to the efficiency of the amplification method, and that a loop of 40 bases or longer gave the best results (page v, column 1). Notomi also teaches that the primers used in the method have an intervening sequence between the (Ac') region and the (B') region (see page ii, column 1, where an intervening sequence that is four nucleotides in length is taught). Since the template-

complementary region of the primers of Rabbani is 19 or 20 nucleotides (see above), separation of the two regions bound by the two portions of these primers by 40 nucleotides as suggested by Notomi would result in (X+Y) values of 59 and 60. These (X+Y) values are greater than 30 as required by claims 1 and 9.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Notomi to the method taught by Rabbani. An ordinary artisan would have been motivated to optimize the length of the loop formed by the primer taught by Rabbani, since Notomi taught that this parameter was critical to achieving optimal amplification efficiency (see page v, column 1). Furthermore, since Notomi taught that a loop of at least 40 nucleotides was optimal to achieving optimal amplification efficiency, application of these teachings to the method of Rabbani would have yielded primers with the claimed X+Y value (see above). Finally, attention is directed to *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) which states, “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” Thus, the methods of claims 1-7 and 9-16 are *prima facie* obvious over Rabbani in view of Notomi.

9. Claims 8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabbani et al. (EP 0 971 039 A2; cited previously) in view of Notomi et al. (Nucleic Acids Research 2000; 28(12): c63; cited previously) and further in view of Kool, E.T. (Current Opinion in Chemical Biology (2000) 4: 602-608; cited previously).

The combined teachings of Rabbani and Notomi result in the methods of claims 1-7 and 9-16, as discussed above.

Neither Rabbani nor Notomi teaches that target nucleic acid sequence in the template nucleic acid comprises non-natural nucleotides as required by claims 8 and 17.

Kool teaches methods of using modified DNA templates as substrates for DNA polymerases. Kool teaches that DNA polymerases can accept synthetic modifications to the template or newly synthesized strand (page 602, column 2). Kool further teaches that templates containing nucleotides with altered hydrogen-bonding capabilities may be amplified by DNA polymerase (page 604). Kool teaches that the presence of these non-native nucleotides in the template strand directs non-specific incorporation of any of the four natural bases into the newly synthesized strand, which is useful for mutagenesis (page 604).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to conduct the amplification method resulting from the combined teachings of Rabbani and Notomi using a template containing non-natural nucleotide. An ordinary artisan would have been motivated to do so, because Kool taught that the inclusion of such nucleotides in the template strand was useful for mutagenesis applications (see page 604). Since Kool further taught a number of specific examples of non-native nucleotides that could be recognized and amplified by DNA polymerases (see pages 604-606), an ordinary artisan would have had a reasonable expectation of success in utilizing a template containing non-native nucleotides in the method resulting from the combined teachings of Rabbani and Notomi. Thus, the methods of claims 8 and 17 are *prima facie* obvious over Rabbani in view of Notomi and further in view of Kool.

***Response to Arguments***

10. Applicant's arguments filed on July 21, 2008 with respect to the rejection of claims 1-7 and 9-16 under 35 U.S.C. 103(a) as being unpatentable over Rabbani in view of Notomi and the rejection of claims 8 and 18 under 35 U.S.C. 103(a) as being unpatentable over Rabbani in view of Notomi and further in view of Kool have been fully considered, but they were not persuasive. Applicant argues that the claimed methods are unobvious, because the use of primers having X+Y values of 30 or more and X-Y/Y values between -1.00 and 1.00 show unexpectedly improved amplification properties, specifically, increased amplification efficiency, relative to primers not satisfying these conditions (see pages 8-11).

This argument and the data provided on page 10 of the response were carefully considered. Based on the data provided by Applicant on page 10 of the response, the evidence of unexpected results does not appear to be commensurate in scope with the claimed invention. Independent claims 1 and 9 are drawn to amplification methods wherein the value of X+Y is 30 or more. It would appear from the data provided by Applicant that at X+Y values greater than 35, the amplification efficiency decreases instead of remaining constant or further decreasing (see primer sets 6-11, 19, and 20). Therefore, the evidence of unexpected results provided by Applicant does not appear to extend over the entire claimed range (X+Y = 30 or more) and furthermore, based on the provided data, one would expect the opposite result, namely decreased amplification efficiency when  $X+Y > 35$ . As noted in MPEP 716.02(d), "Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the 'objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support.' In other words, the showing of unexpected

results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980).

MPEP 716.02(d) also states that “The nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. *In re Kollman*, 595 F.2d 48, 201 USPQ193 (CCPA 1979).” As noted above, the evidence does not suggest that the increased amplification efficiency would extend over the entire claimed range, but rather that amplification efficiency decreases at values of  $X+Y > 35$ . Since the evidence of unexpected results is not commensurate in scope with the claimed invention and since one of ordinary skill in the art would not expect the unexpected results to extend over the entire claimed range, the rejections of claims 1-17 previously made under 35 U.S.C. 103(a) citing Rabbani and Notomi as the primary combination of references have been maintained.

Applicant also argues that Notomi does not teach or suggest limiting the range of  $X+Y$ ,  $X+Y+Y'$ ,  $(X-Y)/X$ , or  $\{X-(Y-Y')\}/X$  (see page 11). This argument was not persuasive, because Notomi expressly taught that the loop size (*i.e.* the  $Y$  value) was a critical parameter requiring optimization, and that loop sizes greater than 40 nucleotides worked especially well (page v, column 2). Notomi also taught suitable lengths for the claimed  $X$  value and for an intervening sequence between regions ( $Ac'$ ) and ( $B'$ ) (*i.e.* the claimed  $Y'$  value) (see page ii). These teachings of Notomi would have suggested to the ordinary artisan that the values of  $X$ ,  $Y$ , and  $Y'$  should be optimized to maximize the desired results (*e.g.* specific and efficient isothermal amplification) using routine experimentation. Since, as discussed above, the evidence of

unexpected results was not commensurate in scope with the claimed invention, the rejection has been maintained.

***Conclusion***

11. No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/  
Primary Examiner, Art Unit 1637

/ANGELA BERTAGNA/  
Examiner, Art Unit 1637